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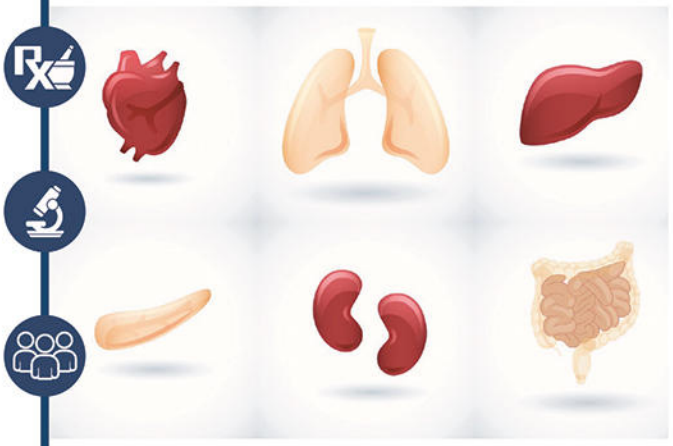

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ORIGINAL ARTICLE

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Impact of machine perfusion after long static cold storage on delayed graft function incidence and duration and time to hospital discharge

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Abstract

Delayed graft function (DGF) is very high in our center (70%-80%), and we usually receive a kidney for transplant after more than 22 hours of static cold ischemia time (CIT). Also, there is an inadequate care of the donors, contributing to a high rate of DGF. We decided to test whether machine perfusion (MP) after a CIT improved the outcome of our transplant patients. We analyzed the incidence of DGF, its duration, and the length of hospital stay (LOS) in patients who received a kidney preserved with MP after a CIT (hybrid perfusion—HP). We included 54 deceased donors kidneys preserved with HP transplanted from Feb/13 to Jul/14, and compared them to 101 kidney transplants preserved by static cold storage (CS) from Nov/08 to May/12. The median pumping time was 11 hours. DGF incidence was 61.1% vs 79.2% ($P = .02$), median DGF duration was 5 vs 11 days ($P < .001$), and median LOS was 13 vs 18 days ($P < .011$), for the HP compared to CS group. The observed reduction of DGF with machine perfusion did not occur in donors over 50 years old. In the multivariate analysis, risk factors for DGF, adjusted for CIT, were donor age (OR, 1.04; $P = .005$) and the absence of use of MP (OR, 1.54; $P = .051$). In conclusion, the use of HP contributed to faster recovery of renal function and to a shorter length of hospital stay.

KEYWORDS
delayed graft function, kidney (allograft) function/dysfunction, organ perfusion and preservation

1 | INTRODUCTION

Delayed graft function (DGF) is an important prognostic factor after transplantation. It is associated with high rates of complications, such as rejection and infections; poorer long-term graft survival; longer hospitalization; and higher costs.[1,2] In Brazil, 50%-80% of renal transplants from deceased donors evolve with DGF,[2-6] compared with low rates reported in transplantation centers of the United States[7] and Europe.[8] This problem in Brazil is mainly due to long cold ischemia time (CIT), generally longer than 20 hours, and inadequate maintenance of donors after brain death diagnosis.[2,4,6] The maintenance of the donor after brain death diagnosis is not often possible in public intensive care units, which are often crowded and lack skilled professionals and/or dedicated staff to care for donors.[4,9,10] In addition, following a worldwide trend, the use of donors with expanded criteria (UNOS ECD system criteria) is increasing; such use currently constitutes 20%-30% of donors in Brazil and might contribute for the increase of DGF rate.[3,6,7,11]

In Brazil, long CIT depends on the logistics of donation and allocation of organs.[4] To reduce the CIT, it is necessary to optimize the

laboratory compatibility testing, the allocation of recipients, and their early arrival at transplant center.[4]

Studies have shown that the use of machine perfusion (MP) provided better results than static cold storage (CS) preservation method in such outcomes as reduced risk for DGF and better graft survival in the first and third years after transplantation. These findings were observed in both standard donor organs and organs from donors with expanded criteria.[8,10,12]

Our institution is located in the state of São Paulo, where 36% of deceased donors kidney transplantations in 2014 were performed in Brazil.[13] Donation after cardiac death has not been accepted in Brazil. In São Paulo, the process of procurement and allocation begins after the State Coordination of São Paulo is notified of a potential brain-dead donor; this Coordination is responsible for the control of patients on the waiting list and allocation of organs. After notification, State Coordination contacts the organ procurement organization (OPO) that acts in the region where the hospital of the donor is located. The OPO is responsible to support all organ procurement processes, clinical evaluation of the donor with confirmation of brain death diagnosis, viability assessment of organs, interview of the family, and donor maintenance care prior to organ recovery.[14,15] Usually, after being contacted by State Coordination, surgical teams extract kidneys, and place them in perfusion solution and melting ice. After release of results compatibility testing, the State Coordination determines which are the respective recipients and forwards the kidneys to the transplantation hospital where recipients are enrolled in the waiting list. Because our hospital is not a recovery center (it does not perform surgical removal), the kidney is delivered, on average, after 22 hours of CIT.

In most centers where the perfusion machine is used, in general, the kidney is placed on a MP in the donors' operating room and they are pumped during the whole cold ischemic time. In contrast, in our transplantation center, the kidney is connected to the MP after a long period of static cold storage that preceded the arrival of the kidney in our institution (Figure 1).

Some experimental studies showed that hybrid perfusion (ie, kidneys that remain in CS and that were subsequently placed in the MP) evolved with improvement of some hemodynamic parameters and better renal function.[16-19] The New York City OPO uses a hybrid strategy for kidneys allocated from a distant procured donor hospital (imported kidneys); these kidneys arrive after a mean CIT of 32 hours in preservation solution and ice and are connected to the MP when they arrive in New York City.[17] However, the employment of machine perfusion following static cold storage vs the use of machine perfusion throughout the entire preservation period is still a matter of debate and recently has been investigated.[20]

The main objective of our study was to evaluate the impact of MP after a long time of CS static perfusion (hybrid perfusion) on DGF rate, length of hospital stay after transplant surgery and dialysis duration, acute rejection within the first 14 days, and renal function at discharge and at 6 months.

As secondary objectives, this study sought to (i) evaluate whether MP hemodynamic parameters, as renal resistance and renal flow correlate with the outcomes (DGF, length of hospital stay after transplant surgery and dialysis duration, acute rejection within the first 14 days and renal function at discharge and at 6 months) and (ii) define the risk factors associated with DGF and kidney function at 6 months in this population.

2 | MATERIALS AND METHODS

This study was carried out at a single center by the kidney transplantation program of the Hospital Israelita Albert Einstein in São Paulo, Brazil. We used a prospective cohort approach and included patients who underwent deceased donor kidney transplantation and that the preservation method used was kidney perfusion machine after a long period of static cold storage, which in this study is called hybrid perfusion (HP); a historic control group consisted of renal transplant recipients of organs from deceased donors exclusively preserved using a static approach (control group; CS).

Inclusion criteria for the HP group were transplantations done between February 2013 (when the hybrid strategy began in our institution) and July 2014. Donors and recipients were all older than 18. After a period of cold storage, donor kidneys were connected to MP in our center. Exclusion criteria for this group were as follows: participation in another trial; kidneys which had been placed on MP in the donors' operating room before the arrival at our center, early graft loss due to surgical causes, and violation of immunosuppression routines. During the study period, we performed 67 kidney transplantations with organs from deceased donors; of these, seven patients were excluded because their kidneys were connected in perfusion machine after the extraction, before the arrival at our center, one because of violation of the immunosuppression routine, one because the patient was younger than 18 years old, and two patients had an early graft loss due to technical renal allograft thrombosis. Therefore, 54 patients were included in the HP group.

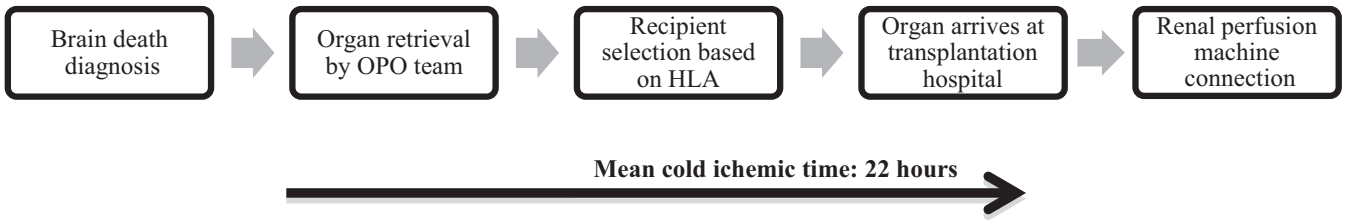

FIGURE 1 Procurement process in the state of São Paulo—Brazil

The historic control group included 101 deceased donor renal transplant patients from November 2008 and May 2012, whose allocated kidneys were submitted to the CS preservation method. Patients who were older than 18 years underwent the procedure in the same institution with the same medical team, and received the same clinical and surgical care and immunosuppression protocol.

This study was approved by the ethical and research committee at our institution. The need for consent was waived because the preservation method was selected before the transplantation and is a step in the routine care delivery to all transplants from deceased donors. Identifier: 36993814.9.0000.0071.

2.1 | Logistics and use of machine perfusion

The kidney arrives at our center after a mean static CIT of 22 hours, preserved in Euro-Collins solution. The transplantation surgical team conducts the back table and then connects the kidney to the perfusion machine (LifePort Kidney Transporter [Organ Recovery Systems, Chicago, IL USA]), which is monitored by the nursing team. According to our institution's protocol, the kidney remains in the perfusion machine for at least 6 hours. Based on the experience of New York City OPO,[17] the perfusion solution KPS-1 is used in the perfusion machine, and as initial parameter, a 30-mm Hg systolic pressure of perfusion is maintained at a temperature about 1-8°. While the kidney is in the perfusion machine, we monitored and recorded the flow and intrarenal resistance in real time at 0 hours, 1 hour, 6 hours, and when the kidney was disconnected from the machine (final).

2.2 | Immunosuppression protocol

All patients in both groups received induction with one intraoperative dose of thymoglobulin, 1.5 mg/kg body weight, followed by sequential doses of 1.0 mg/kg body weight according to CD3 cell counts, as previously reported.[21] The maintenance immunosuppression regimen was composed of tacrolimus (0.1 mg/kg body weight every 12 hours), prednisone (0.5 mg/kg body weight), and mycophenolate sodium (720 mg every 12 hours). Calcineurin inhibitor therapy was initiated after antithymocyte globulin suspension. All patients received prophylaxis with trimethoprim-sulfamethoxazole up to 6 months after transplantation. There was no other protocol change between both groups in this study.

2.3 | Data collection

Data were collected retrospectively from electronic medical records for the control group (CS) and in real time for the HP group using a specific form created to monitor these patients.

2.4 | Analyzed outcomes

Outcomes analyzed were delayed graft function (defined as the need for dialysis in the first week after transplantation), primary nonfunction, duration of DGF in days, acute rejection within the first 14 days, length of hospital stay, renal function (measured by creatinine and by glomerular filtration rate [GFR] as estimated by the Modification of Diet in Renal Disease equation) at discharge and at 6 months.

2.5 | Data analysis

Numerical variables with normal distribution by the Shapiro-Wilk test were described as means and standard deviations; non-normally distributed variables were described as medians and interquartile ranges and as minimal and maximal values.

Groups were compared in relation to observed variables. For normally distributed variables, the comparison was performed using the Student *t*-test; data not normally distributed were compared in groups using the Mann-Whitney *U* test. Categorical variables were compared by chi-squared test or Fisher's exact test depending on the number of individuals in each class.

We verified the association between final renal flow and final renal resistance within the perfusion circuit of machine perfusion with several variables using linear regression models and logistic regression.

Subanalyses were performed to evaluate the benefit of the use of the machine on outcomes (DGF, time of DFG, renal function, length of hospital stay) in some subgroups of patients according to some characteristics of donors considered to be present as high risk for DGF, such as the donor age older than ≥50 years and according to the expanded criteria.

Variables previously selected by the researcher were tested, including risk factors for DGF and GFR at 6 months in the univariate analysis. Only variables with *P* value lower than .20 in a univariate analysis were considered for multivariate analysis. Selection for the multivariate model was carried out using the stepwise method and as selection criterion of variables of AIC along with the residue analysis, always controlled by static ischemia time. Results for DGF were obtained using logistic regression models. Results for estimated GFR (eGFR) were achieved using Gaussian linear regression models.

Relationships between pumping time, final renal resistance, and DGF were investigated using the Mann-Whitney *U* test. The association between pumping time and renal function was determined using the Spearman correlation coefficient.

Results are presented as estimated coefficients, 95% confidence intervals, and *P* values. Level of significance adopted was 5%. Analyses were performed using the R package (R Core Team, 2013).

3 | RESULTS

3.1 | Clinical and demographic characteristics of donors and recipients, transplant characteristics, and hemodynamic parameters of machine perfusion

Clinical and demographic characteristics of recipients and donors, transplant characteristics, and hemodynamic parameters of MP are described in Table 1. Recipients in the HP group were younger than those in the CS group (44.5 years vs 55 years; *P* = .006). No significant differences were observed for the other demographic characteristics.

TABLE 1 Characteristics of donors and recipients, transplant characteristics, and hemodynamic parameters of machine perfusion

Variables	CS group (n = 101)	HP group (n = 54)	*P* value
Recipient characteristics			
Median recipient age (years)	55.00 [45.00, 60.00]	44.50 [37.25, 54.75]	.006
Recipient gender			
Male	67 (66.3%)	30 (55.6%)	.223
Median duration of pretransplantation dialysis (months)	54.00 [30.00, 87.00]	35.50 [13.00, 90.25]	.057
Cause of chronic renal disease			
Hypertension	20 (19.8%)	4 (7.4%)	.053
Diabetes	18 (17.8%)	8 (14.8%)	
GN	9 (8.9%)	8 (14.8%)	
Polycystic disease	16 (15.8%)	4 (7.4%)	
Other	38 (37.6%)	30 (55.6%)	
Median PRA (%)	0.00 [0.00, 0.50]	0.00 [0.00, 0.00]	.805
Median HLA mismatches	3.00 [2.00, 4.00]	3.00 [2.00, 3.00]	.997
Donor characteristics			
Donor age (years)	43.00 [29.00, 52.00]	42.50 [27.25, 50.75]	.492
Donor gender			
Male	56 (55.4%)	33 (61.1%)	.609
Donor hypertension			
Yes	35 (35.0%)	15 (28.3%)	.47
Donor cause of death – CVA			
Yes	53 (52.5%)	23 (42.6%)	.312
Donor terminal creatinine (mg/dL)	1.32 [0.99,1.97]	1.30 [0.88, 1.83]	.604
Expanded criteria donor			
Yes	29 (28.7%)	10 (18.5%)	.18
Ischemic times			
Median static cold ischemic time (hours)	22.00 [20.00, 23.00]	20.00 [17.00, 22.00]	.017
Median pumping perfusion time (hours)	-	11.00 (9.25, 13.75)	-
Median total ischemic time (static + pumping) (hours)	22.00 [20.00, 23.00]	31.50 [28.00, 34.00]	<.001
Hemodynamic machine parameters			
Median initial flow (mL/min)	-	55.00 [38.25. 69.00]	-
Mean 1 h flow (mL/min)	-	94.78 (31.24)	-
Mean 6 h flow (mL/min)	-	98.15 (28.27)	-
Mean final flow (mL/min)	-	102.91 (30.37)	-
Median initial resistance (mm Hg/mL/min)	-	0.46 [0.39, 0.66]	-
Median 1 h resistance (mm Hg/mL/min)	-	0.26 [0.22,0.32]	-
Median 6 h resistance (mm Hg/mL/min)	-	0.23 [0.21, 0.30]	-
Median final resistance (mm Hg/mL/min)	-	0.23 [0.20, 0.30]	-

Median values are reported with interquartile range.

Among transplant variables, we observed that the HP group had a shorter duration of static cold storage time (20 vs 22 hours; $P = .017$) and longer duration of total CIT (31.5 vs 22 hours; $P = .017$). The mean pumping time was 11 hours (25% and 75% interquartile range, 9.25 and 13.75 hours). The pumping time was approximately half the time of CS (median, 20 hours; 25% and 75% interquartile range, 17 and 22 hours). No other significant differences between the two groups were seen.

3.2 | Comparison of outcomes between the cold storage and hybrid perfusion groups

None of the groups presented primary nonfunction. The use of the HP significantly reduced the incidence of DGF: 79.2% in the CS group and 61.1% in the HP group ($P = .022$). The duration of dialysis after transplantation was reduced from 11 to 5 days ($P < .001$), and the length

TABLE 2 Comparison of outcomes between cold storage (CS) and hybrid perfusion (HP) groups

	CS group n = 101	HP group n = 54	*P* value
Recipient outcomes			
Primary nonfunction	0	0	-
Delayed graft function			
No	21 (20.8%)	21 (38.9%)	.022
Yes	80 (79.2%)	33 (61.1%)	
Length of DGF	11.00 [7.00, 15.00]	5.00 [1.00, 10.00]	<.001
Acute rejection within 14 d after transplantation			
No	90 (89.1%)	48 (88.9%)	.578
Yes	11 (10.9%)	6 (11.1%)	
Median length of hospital stay (days)	18.00 [12.00, 24.00]	13.00 [8.25, 16.75]	<.001
Median discharge eGFR (mL/min)	26.08 [18.26, 36.19]	32.65 [18.52, 45.95]	.254
Median eGFR at 6 mo (mL/min)	57.41 [44.60, 72.76]	55.00 [43.00, 65.60]	.256

Median values are reported with interquartile range.

of hospital stay decreased from 18 to 13 days ($P < .001$) in HP. Acute rejection rate within the first 14 days, renal function at discharge and at 6 months did not significantly differ between groups (Table 2).

3.3 | Hemodynamic parameters in hybrid perfusion group

The two hemodynamic parameters evaluated were intrarenal flow (F) and intrarenal resistance (R), described in Table 1. F increased from 55 to 102.9 mL/min, whereas R decreased from 0.46 to 0.23 while the kidney remained in the MP. For both parameters, the variation was greater during the first hour of placement in the MP (Table 1).

Considering the association between the final renal flow and outcomes, for each unit increase in the final renal flow, we expect a 0.210 mL/min increase in the discharge creatinine clearance value ($P = .021$) and 0.237 mL/min in the creatinine clearance value in 6 months ($P = .035$).

We also analyzed the association between the final resistance and outcomes. For each increase of 0.1 units in the final renal resistance, we expect an increase of 1.5 days in DGF ($P = .009$). For each increase of 0.1 unit increase in final resistance, we expect a decrease of 4.101 mL/min in the discharge creatinine clearance value ($P = .022$) and a decrease of 6.307 mL/min in the clearance of creatinine value of 6 months after transplantation ($P = .013$).

3.4 | Subanalyses of risk groups

In the subgroup of donors aged ≥50 years, patients in the HP group (n = 16) had a shorter hospital stay (10.50 vs 22 days; $P = .006$) and shorter dialysis duration (4.00 vs 12.50 days; $P = .023$) than CS group (n = 35). In this subgroup, the HP did not reduce the DGF rate.

In the subgroup analysis consisting only of expanded criteria donors, 10 patients were included in HP group vs 29 patients in CS group, and no difference in outcomes was seen when CS and HP groups were compared.

3.5 | Factors associated with delayed graft function

In univariate analysis, risk variables statistically significant associated with DGF were donor age (OR, 1.04; $P = .002$), CIT (OR, 1.14; $P = .011$), cerebrovascular accident as the cause of the donor death (OR, 2.12; $P = .045$), donor with hypertension (OR, 2.59; $P = .030$), and expanded criteria donor (OR, 3.19; $P = .026$). The pumping time (OR, 0.93; $P = .013$) and belonging to the HP group (OR, 0.41; $P = .017$) decreased the DGF risk (Table 3).

In multivariate analysis, adjusted for static cold ischemic time, independent risk factors for DGF were donor age (OR, 1.04; $P = .005$) and belonging to the HP group (OR, 0.46; $P = .051$). Therefore, for each year of increase in donor age, there was a 4% increase in the chance of DGF. In addition, belonging to the HP group decreased the chance of DGF by 54% after adjustment for variables included in this model (Table 3).

3.6 | Factors associated with glomerular filtration rate at 6 months

In the univariate analysis, risk factors significantly associated with worse renal function at 6 months were expanded criteria donor, donor age ≥50 years, cerebrovascular accident as the cause of donor death, donor with hypertension, recipient's age, and DGF (Table 4). In the multivariate analysis, adjusting for static cold ischemic time, both cerebrovascular accident as the cause of donor death ($P < .001$) and donor age ≥50 years ($P = .027$) were variables of risk for worse renal function at 6 months (Table 4).

4 | DISCUSSION

This study showed that use of MP after a period of cold static ischemia, in the HP group, reduced the DGF rate compared with the CS group (79.2% vs 61.1%; $P = .022$). In addition, in the multivariate

TABLE 3 Univariate and multivariate analysis: risk factors for delayed graft function (DGF)

Variable	Estimate	OR	P value
Univariate analysis			
Donor age	0.04	1.04	.002
Cold static ischemic time (hours)	0.13	1.14	.011
Pumping time (hours)	−0.07	0.93	.013
HP group (yes)	−0.89	0.41	.017
Expanded criteria donor (yes)	1.16	3.19	.026
Donor hypertension (yes)	0.95	2.59	.030
Cause of donor death—CVA (yes)	0.75	2.12	.045

	Estimate	OR	CI		P value
Multivariate analysis					
Cold ischemic time	0.10	1.10	1.00	1.22	.053
Donor age (years)	0.04	1.04	1.01	1.07	.005
HP group (yes)	−0.77	0.46	0.21	1.01	.051

analysis the use of the HP reduced the DGF risk (OR, 0.46; CI, 0.21-1.01; $P = .051$). The duration of dialysis and hospitalization was also lower in the HP group (median: 11 vs 5 days [$P < .001$] and 18 vs 13 days [$P < .001$]), respectively. Therefore, the HP group presented faster recovery of graft function, such as reported by other authors who compared MP and CS preservation methods.[8] In a previous study, Sandes-Freitas et al categorized patients in quartiles according to duration of DGF and they showed that the highest quartile, which was named as prolonged DGF (>15 days), had a negative impact on graft function, patient and graft survival at 1 year. In addition, the prolonged DGF was an independent risk factor to graft loss (OR: 3.876 $P < .001$) and death (OR: 3.065 $P = .001$); therefore, the longer the DGF duration, the worse the graft and the patient survivals will be.[22] Considering this, as the HP group in our study reduced the duration of DGF from 11 to 5 days, this might be considered an additional benefit of HP strategy, to prevent the damage associated with prolonged DGF on graft and patient survivals.

As transplantations with organs from donors aged ≥50 years and transplants from expanded criteria donors are associated with worse outcomes after transplantation, such as higher rates of DGF and lower graft survival,[23] we performed a subanalysis considering only donors aged ≥50 years and expanded criteria donors. A subanalysis including only expanded criteria donors showed that the use of HP did not improve results after the transplantation. This result differs from findings in other studies showing that MP reduced the DGF rate and improved 1-year graft survival in expanded criteria donors.[24,25] On the other hand, in the subanalysis of donors aged ≥50 years, the use of the HP did not reduce the DGF rate, but the duration of DGF was lower than in the control group, which might have a positive impact in long-term results. The lack of benefits with related to the use of MP after a long CIT in transplants from expanded criteria donors may be due to these kidneys are more susceptible to ischemic injury in general, they have lower renal mass, more chronic histologic injuries, and lower ability for repair and regeneration.[23] However, we must consider that these subanalysis involved a small sample of patients. Recently, Gallinat et al performed a study where they compared the results of expanded criteria donors kidneys from the same donor, one of them being preserved in cold storage and the other in perfusion machine after a period of cold storage (mean pumping time: 5.5 hours, mean cold ischemic time in CS group: 12.1 hours, and mean cold ischemic time in MP group: 13.4 hours). The authors observed a lower rate of primary nonfunction in HP group (0% vs 9.3%), and they have showed that the HP strategy was an independent factor for prevention of DGF

TABLE 4 Univariate and multivariate analysis for risk factors for estimated GFR (eGFR) at 6 mo

		Confidence interval		
	Coefficient	Lower	Upper	P value
Univariate analysis				
Expanded criteria donor (yes)	−17.85	−25.91	−9.78	.0001
Donor age ≥50 y	−18.45	−25.72	−11.19	.0001
Donor CVA (yes)	−11.33	−18.58	−4.08	.002
Donor hypertension (yes)	−11.49	−19.28	−3.71	.004
Recipient age	−0.30	−0.58	−0.02	.035
DGF	−8.94	−17.34	−0.54	.037

		Confidence interval		
	Estimate	Lower	Upper	P value
Multivariate analysis				
Cold static ischemic time (hours)	−0.76	−1.66	0.13	.097
Donor CVA (yes)	−7.85	−14.79	−0.91	<.001
Donor age ≥50 y	−15.91	−23.27	−8.56	.027

(OR:0. 28, P = .041), as our study has also observed. The DGF rate was lower in HP group (20.9% vs 11.6%), and graft and patient survivals at 1 year were slightly better in HP group, however, without statistical significance. The authors believe the pulsatile stimulation of the renovasculature is an important reason for these results. It might preserve the vascular endothelium and its phenotype, preventing transcription of inflammatory and vasoconstrictors factors.[20]

Although the total CIT was significantly longer in the HP group, 22 vs 31.5 hours (P < .001), with 11 hours on perfusion machine, no harm to the graft was seen with use of the HP. Our protocol for the perfusion machine use requires a minimum of 6 hours, but the mean time in this study was 11 hours due to logistic reasons, that is, we were able to wait for patients who lived in distant regions and to avoid transplant surgery at dawn hours.

This result corroborates with that of a previous study showing that use of MP may extend the total CIT without injuring the graft.[20,24,26-28] When we evaluated the effect of HP on DGF in a univariate analysis, pumping time had a protective effect on DGF, that is, for each 1-hour increase in the pumping time, the risk of DGF decreased 7% (OR, 0.93; P = .013), data not shown. Of importance, there was no difference among both groups between total doses of thymoglobulin, day of initiation of tacrolimus, and its levels at 15, 30, 90, and 180 days post-transplantation (data not shown). In addition, a study using data from the Scientific Registry of Transplant Recipients (SRTR) comparing these two perfusion strategies (CS vs MP) reported that the longer the pumping time, the lower the DGF risk is.[24] We believe that the effect of pumping time might be associated with an improvement of hemodynamic parameters, reduction of oxidative and metabolic stress, and consequently vascular injury.[29] In addition, MP probably reduces the graft susceptibility to warm ischemic time and reperfusion injuries related in the graft.[18] In addition, Gallinat et al[30] have also showed in experimental porcine model that MP may reduce the damage to the endothelial cell and preserve the parenchymal integrity.

Considering hemodynamic parameters of the machine, after an hour of machine perfusion use, an important decrease in vascular renal resistance was seen (from 0.46 to 0.26 mm Hg/mL/min) and a significant increase in renal flow occurred (from 55 to 99.8 mL/min); these changes are similar to those reported in a previous study.[27] We observed no significant differences in hemodynamic parameters measured in subsequent hours. Variations in flow and vascular renal resistance can be directly associated with hemodynamic effect of MP related to renal vasodilatation and the capability of this graft to respond to this effect. Grafts with vascular changes mainly associated with aging and vascular disease probably have a lower response to the hemodynamic effect of machine perfusion. In our study, both final renal flows as the final vascular renal resistance were associated with renal function at discharge and at 6 months, directly and inversely, respectively. However, in multivariate analysis, these two variables were not associated with DGF or GFR risk at 6 months. However, this lack of association is different from the findings in other studies that showed final vascular renal resistance as a risk factor for DGF and graft loss after 1 year.[31] Either DGF or eGFR are multifactorial dependent; therefore, in our models others variables were more important as risk factors for DGF and eGFR than the hemodynamic parameters.

In multivariate analysis, belonging to HP group did not impact the renal function at 6 months. In our study, renal function at 6 months was associated only with donor age and the presence of cardiovascular disease. Of importance, there was no difference among both groups, HP vs CS, in renal function (data not shown). Other studies also found no difference in short- and long-term renal function after transplantation between the two preservation strategies.[8,10,32] In our model, the variables related to the quality of the donor, as age and presence of cardiovascular disease, were more determinants for renal function. The preservation and ischemic injuries in the kidneys of older donors may be less responsive to the benefits of HP. However, during the first 6 months after transplantation, a variety of injuries still occurring in the graft, such as those related to higher doses of immunosuppressors, immunologic, opportunistic infections, can mask the benefit of machine perfusion in this period.

Our results should be interpreted with caution because we used a small sample of patients in HP group, we did not use a randomized approach, and we retrospectively analyzed the control group. In addition, other factors that cannot be disregarded are the concomitant use of MP with a perfusion solution, which is well recognized as more efficient than Euro Collins, such as KPS-1, the control group used Euro Collins solution for preservation, which is associated with higher DGF rate.[31-33] The Euro Collins solution is used even less in US and European centers, but it is still commonly used in Brazil because of its lower cost.[34] The use of this solution is considered another reason that may contribute to our high rates of DGF.

In conclusion, our study showed that it is possible to use machine perfusion after a long period of static cold ischemia to reduce the risk and rate of DGF and the duration of DGF thereby enabling faster recovery of graft function, avoiding the damage related to DGF and prolonged DGF. The observed reduction of DGF with machine perfusion did not occur in donors over 50 years old.

In addition, using the support of hemodynamic parameters, it is possible to predict how graft function will evolve. Because of the rules and current conditions for the organ procurement system in Brazil, it is not possible to reduce the time of static cold storage ischemia; therefore, the use of a machine after long CS can be an alternative to improve graft quality and transplantation results. A randomized study comparing the two strategies and including a large sample of patients can confirm these results and long-term effects. A cost-effectiveness analysis should be also considered to help the federal government make a decision in favor of purchasing perfusion machines for the public health system.

CONFLICT OF INTEREST

None.

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